

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/043660

A. CLASSIFICATION OF SUBJECT MATTER

A61K38/06 A61P43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|---|
| X | US 5 382 679 A (GALZIGNA ET AL) 17 January 1995 (1995-01-17) | 58,62, 67,71, 76,80, 85,89 |
| Y | the whole document | 1-10, 20-39, 46-51, 57, 59-61, 68-70, 77-79, 86-88, 94,95 |
| | ----- -/- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

8 September 2005

Date of mailing of the international search report

15. 12 2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|--|
| X | WO 02/090314 A (GALILEO LABORATORIES, INC; WANG, BING; MILLER, GUY; FLAIM, STEPHEN, F;) 14 November 2002 (2002-11-14) *Formula Ig and Formula Ih*examples 15,16 ----- | 58,62, 67,71, 76,80, 85,89 |
| X | US 6 197 749 B1 (HAMURO JUNJI ET AL) 6 March 2001 (2001-03-06) *formula I* column 7 ----- | 58,62, 67,71, 76,80, 85,89 |
| X | KLEINMAN W A ET AL: "Status of glutathione and other thiols and disulfides in human plasma." BIOCHEMICAL PHARMACOLOGY. 1 JUL 2000, vol. 60, no. 1, 1 July 2000 (2000-07-01), pages 19-29, XP002343366 ISSN: 0006-2952 cited in the application page 21, column 1, paragraph 4 ----- | 58,59, 62,67, 68,71, 76,77, 80,85, 86,89 |
| X | SATO S ET AL: "Identification of thioether intermediates in the reductive transformation of gonyautoxins into saxitoxins by thiols." BIOORGANIC & MEDICINAL CHEMISTRY LETTERS. 21 AUG 2000, vol. 10, no. 16, 21 August 2000 (2000-08-21), pages 1787-1789, XP002343367 ISSN: 0960-894X cited in the application *scheme 1* page 1788 ----- | 58,62, 67,71, 76,80, 85,89 |
| Y | WO 98/29375 A (YISSUM RESEARCH AND DEVELOPMENT COMPANY OF THE HEB; MOR - RESEARCH APP) 9 July 1998 (1998-07-09) the whole document ----- | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| A | EP 0 494 405 A (NB INTERNATIONAL TECHNOLOGIES A PARTNERSHIP ORGANISED UNDER THE LAWS O) 15 July 1992 (1992-07-15) ----- -/-- | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|--|
| Y | WO 01/80832 A (OREGON HEALTH SCIENCES UNIVERSITY; GOVERNMENT OF THE UNITED STATES, D/) 1 November 2001 (2001-11-01) the whole document | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| A | WO 02/17962 A (OREGON HEALTH AND SCIENCE UNIVERSITY; NEUWELT, EDWARD, A; MULDOON, LES) 7 March 2002 (2002-03-07) | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| A | US 6 369 106 B1 (ATLAS DAPHNE ET AL) 9 April 2002 (2002-04-09) | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| Y | US 5 824 693 A (GOLDBERG ET AL) 20 October 1998 (1998-10-20) the whole document | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| Y | EP 0 572 110 A (CLINTEC NUTRITION COMPANY) 1 December 1993 (1993-12-01) the whole document | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|--|
| A | EP 0 501 641 A (CLINTEC NUTRITION COMPANY) 2 September 1992 (1992-09-02) | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| A | ----- US 6 586 404 B1 (DEMOPOLIS HARRY B ET AL) 1 July 2003 (2003-07-01) | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| Y | ----- NAGASAWA H T ET AL: "Protection against acetaminophen-induced hepatotoxicity by L-CySSME and its N-acetyl and ethyl ester derivatives." JOURNAL OF BIOCHEMICAL TOXICOLOGY. 1996, vol. 11, no. 6, 1996, pages 289-295, XP008051903 ISSN: 0887-2082 the whole document | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| A | ----- PURDIE J. W.: "Gamma-Radiolysis of Cysteine-Cysteamine Disulfide in Aqueous solution" CANADIAN J. OF CHEMISTRY, vol. 49, 1971, pages 725-730, XP008051946 the whole document | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |
| T | ----- WO 2005/025570 A (DIAMEDICA INC; LAUTT, WILFRED WAYNE) 24 March 2005 (2005-03-24) ----- | 1-10, 20-39, 46-51, 57-62, 67-71, 76-80, 85-89, 94,95 |

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-10, 20-39, 46-51, 57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

33-39 (partially), 1-10, 20-32, 46-51, 57-62, 67-71, 76-80, 85-89, 94, 95

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10,20-32, 46-51,57-62,67-71,76-80,85-89,94,95 and partially 33-39

Pharmaceutical composition or the use of a sulphydryl protected glutathione prodrug for the treatment of diseases associated with oxidative stress in a cell, in particular drug induced hepatotoxicity.

2. claims: 11-19, 40-45,52-56,63-66,72-75,81-84,90-93,96-104 and partially 33-39

Pharmaceutical composition or the use of a sulphydryl protected cysteine prodrug (CySSMA) for the treatment of diseases associated with oxidative stress in a cell, in particular drug induced hepatotoxicity.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/043660

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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Information on patent family members

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| WO 2005025570 | A | 24-03-2005 | NONE |